

Publish and be damned

As the pharmaceutical industry faces growing public demand for greater transparency in the publication of drug trial results, Nic Paton asks **Christine-Lise Julou** of the EFPIA about the risks of misinterpretation and the need to respect commercial confidentiality.

The headline in the *British Medical Journal* in October 2010 could barely have been starker: “Patients and doctors are being misled by published data on medicines”. The study it referred to, by a group of researchers at the German Institute for Quality and Efficiency in Health Care, argued that the drug reboxetine was, overall, an ineffective and potentially harmful antidepressant.

Even more worrying for the pharmaceutical industry, it concluded that nearly three-quarters of the data on patients who took part in trials of reboxetine had not been published until then, and that published data on the drug had overestimated the benefits and underestimated the harms of treatment, “all underlining the urgent need for mandatory publication of all clinical trial results”.

Christine-Lise Julou

Christine-Lise Julou is director of the scientific technical and regulatory affairs department at the EFPIA. Prior to this she was senior director regulatory affairs at Rhône-Poulenc Rorer (then Aventis) and Gencell.



So, was this a clear-cut case of ‘nasty Big Pharma’ trying to pull the wool over the eyes of an unwitting public and, in the process, making a fast buck?

Absolutely not, says Christine-Lise Julou, director, scientific and regulatory affairs at the European Federation of Pharmaceutical Industries and Associations (EFPIA): “It’s not so much about people withholding information, it’s about an increased appetite for information. This has to be recognised and acknowledged.”



Nevertheless, for the EFPIA and other organisations, such as the International Federation of Pharmaceutical Manufacturers & Associations, the Japan Pharmaceutical Manufacturers Association and the Pharmaceutical Research and Manufacturers of America, this creates a potential headache.

Clearly, although pharmaceutical companies want and need to respond to this new climate of transparency as best they can, an information free-for-all would have serious ramifications, not only for issues around commercial confidentiality, but also in terms of ensuring the public get accurate and robust information about trial results and the efficacy of the drugs coming through R&D pipelines. Between them, the four organisations have published a number of joint position papers, and continue to monitor how the landscape is evolving in regards to this area.

Great expectations

Legislation in Europe and the US has been in place for some time, but the environment has evolved in the past 20 years or so, as have the expectations of patients and consumers, according to Julou.

“People used to be quite happy for the benefit and risk assessment of drugs to be left to the regulators,” she says. “The industry and regulators were, as a result, not very transparent

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and did not particularly need to be. They were not required to give a huge amount of detail on everything. But expectations have changed, and people want to be better informed.”

Another issue for industry sponsors is the complexity of seeking to publish results of clinical trials in peer-reviewed scientific literature, while needing to place information on multiple databases worldwide. Finding the appropriate information on these multiple databases and literature sources can be complex. Yet Julou feels that the regulations already in place are both robust and adequate; for example, in Europe there are already public databases and procedures in place to populate them.

The EFPIA's involvement

The EFPIA has published two position papers in conjunction with the International Federation of Pharmaceutical Manufacturers & Associations, the Japan Pharmaceutical Manufacturers Association and the Pharmaceutical Research and Manufacturers of America.

Both documents, *Joint Position on the Publication of Clinical Trial Results in the Scientific Literature* (June 2010) and *Updated Joint Position on the Disclosure of Clinical Trial Information via Clinical Trial Registries and Databases* (November 2009), outline a series of principles regarding the disclosure of information relating to clinical trials that the organisation has pledged to commit to, and which they have urged all sponsors of clinical trials to commit to as well.

In addition to this, the EFPIA has stressed that it and the rest of pharmaceutical industry will “continue to work to meet the public demand to have access to enhanced, reliable and informative results on clinical trials concerning medicinal products”.

Latest regulations

In Europe, the requirements concerning the submission of clinical results to regulatory authorities are outlined in Directive 2001/83/EC and Regulation (EC) No 726/2004.

It is already a requirement that all data, positive and negative, is submitted to regulatory authorities. The requirements relate to the submission of the protocols and results to regulatory authorities, the assessment of these by regulatory authorities and the posting of study results on publicly accessible websites, says the EFPIA.

There are specific provisions that apply to medicinal products for paediatric use outlined in Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006, in particular in Article 41.

The German Medical Products Act also contains a number of national provisions, while in the US, the regulatory framework is outlined in the Food and Drug Administration Amendments Act of 2007.

Overall, there is no legal obligation in relation to publication in peer-reviewed journals. However, where study results are published in a peer-reviewed journal, they must not be deemed to be promotional or to suggest that a product may be used for an indication or a population in which the regulatory authorities have not (or not yet) approved its use.

“The regulations are already very broad and do not need to be tougher,” she says. “It is important to respect commercial confidentiality and to not have a negative impact on the pharmaceutical R&D that delivers new medicines for patients. We would have some concerns if there was a proposal to make all information on trials available before a product has been authorised for public use – there is no reason for that.

“While we support enhanced transparency within clinical trials information, it is important to maintain privacy for personal data and protection of commercial and contractual interests so as not to undermine the incentive for research,” she adds.

Support and accuracy

There are important clinical benefits associated with making clinical trial information more widely available, says Julou, but information shouldn't just be available on public websites; it also needs to appear in peer-reviewed journals in order to facilitate proper scientific discussion.

The information that the public can access needs to provide an accurate report of the trial findings, including adverse events. However, there are concerns that if this information isn't put into context, or is viewed by individuals without the appropriate knowledge and experience to understand it, it could be misinterpreted. ■

